Mortality in Relation to Changes in a Healthy Aging Index: The Health, Aging and Body Composition Study

Matthew DL O'Connell,PhD[1,2,3], Megan M Marron,MS[1], Robert M Boudreau, PhD[1], Mark Canney,MBBS,PhD[2], Jason L Sanders,MD,PhD[4], Rose Anne Kenny,MD[2], Stephen B Kritchevsky,PhD[5], Tamara B Harris,MD[6], Anne B Newman,MD,MPH[1]

[1]Center for Aging and Population Health, Department of Epidemiology, Graduate School of Public Health, University of Pittsburgh, PA, USA

[2]The Irish Longitudinal Study on Ageing, Trinity College, Dublin, Ireland

[3]Unit of Academic Primary Care, Warwick Medical School, University of Warwick, Coventry, UK

[4]Department of Medicine, Massachusetts General Hospital, Boston, MA, USA

[5]Sticht Center for Healthy Aging and Alzheimer's Prevention, Wake Forest School of Medicine, Winston-Salem, NC, USA

[6]National Institute on Aging, Bethesda, MD, USA

Corresponding Author: Matthew DL O'Connell, The Irish Longitudinal Study on Ageing (TILDA), Lincoln Gate, Trinity College Dublin, Dublin 2, Ireland. Tel.: +353 1 896 4392; Fax: +353 1 896 245; E-mail: oconnem8@tcd.ie

Abstract

Background: Baseline scores on a Healthy Aging Index (HAI), including 5 key physiological domains, strongly predict health outcomes. This study aimed to characterize 9-year changes in a HAI and explore their relationship to subsequent mortality.

Methods: Data are from the Health, Aging and Body Composition study of well-functioning adults aged 70-79. A HAI, which ranges from 0-10, was constructed at year 1 and year 10 of the study including systolic blood pressure, forced expiratory volume, digit symbol substitution test, cystatin C and fasting glucose. The relationships between the HAI at year 1 and year 10 and the change between years and subsequent mortality until year 17 were estimated from Cox proportional hazards models.

Results: 2264 participants had complete data on a HAI at year 1, of these 1122 had complete data at year 10. HAI scores tended to increase (i.e., get worse) over 9-year follow-up, from (mean (SD)) 4.3 (2.1) to 5.7 (2.1); mean within person change 1.5 (1.6). After multivariable adjustment HAI score was related to mortality from year 1 (Hazard Ratio (95% Confidence Interval) =1.17 (1.13 - 1.21) per unit) and year 10 (1.20 (1.14 - 1.27) per unit). The change between years was also related to mortality (1.08 (1.02 - 1.15) per unit change).

Conclusions: HAI scores tended to increase with advancing age and stratified mortality rates among participants remaining at year 10. The HAI may prove useful to understand changes in health with aging.

Key words: Successful Aging, Epidemiology, Mortality, Physiology

Introduction

Comorbidity indices summarize overall burden of chronic conditions and can identify older adults with the greatest health needs (1). The Healthy Aging Index (HAI) extends this approach using 5 easily measured physiological indicators sensitive to both clinical and subclinical changes in organ structure and function (2). The HAI stratifies the full range of mortality rates and may distinguish those with low from usual rates as an intermediate endpoint for longevity (3)

Many recent observations support the use of the HAI as a summary measure of physiologic aging. The HAI predicts mortality independently of chronological age and comorbidity (2). This finding has been replicated across several samples and population subgroups, including those with minimal diagnosed comorbidity (4-6). The HAI has also been shown to predict onset of disability in well-functioning older adults and future cardiovascular disease in adults aged 60 and over (2, 4). It has also been related to future decline in gait speed (7).

Further studies have shown heritability in HAI scores among long-lived families and identified potential genetic correlates (5, 8). Most recently, HAI scores have been associated with differential metabolite profiles relevant to various age-related pathways and predictive of cardiovascular mortality (9).

These findings show potential utility for the HAI as a surrogate measure of longevity for use in future trials targeting aging (10). Before this can happen, it is vital to establish how the HAI changes with chronological aging and to what extent these changes reflect variations in physiologic aging. A small number of studies have explored trajectories of related healthy aging

measures (11, 12). However, the relationships between changes in these measures and subsequent health outcomes are unclear.

This study aimed to characterize 9-year changes in the HAI in well-functioning adults aging from their 70s to their 80s. Further, we sought to compare the change in HAI score to the score at a given time-point as a predictor of mortality.

Methods

Participants

The Health, Aging and Body Composition (Health ABC) Study is a prospective cohort study of 3,075 nondisabled black (41.7%) and white men and women (51.5%) from the Pittsburgh, PA and Memphis, TN areas, aged 70–79 years at baseline. Eligibility criteria included, no self-reported difficulty walking a quarter mile, climbing 10 steps, or performing mobility-related activities of daily living, no reported use of a walking aid, no history of cancer treatment in the past 3 years, and no plans to move from the area in the next 3 years. The institutional review boards of the University of Pittsburgh, the University of Tennessee, the University of California–San Francisco Coordinating Center, and the National Institute on Aging approved the study and all participants gave informed consent.

Healthy Aging Index

The HAI was constructed as previously described at year 1 and year 10 using markers of cardiovascular, lung, cognitive, metabolic and kidney function (2). Kidney biomarkers were measured using different assays at year 1 compared to later years. To avoid potential inter-assay variability, cystatin C measured at year 3 was used for the year 1 score (13). The study also changed from desktop to handheld spirometers in year 10. Although concerns have been raised over comparability of different devices (14), the 2 models used in Health ABC have been found to give very similar readings (15). All components were scored from 0-2 from most to least healthy using tertiles or clinical cut-points (2, 3). Cut-points for 4 of the components were

previously reported (2), cystatin C tertiles were defined based on the year 3 data. The specific components were:

Systolic Blood Pressure (SBP): 0: <126 mmHg, 1: 126–142 mmHg, and 2: ≥142 mmHg.

Forced Vital Capacity (FVC): men, 0: ≥3,700 mL, 1: 3,066–3,700 mL, 2: <3,066 mL; women, 0: ≥2,564 mL, 1: 2,127–2,564 mL, and 2: <2,127 mL.

Digit Symbol Substitution Test (DSST): 0: ≥42 points, 1: 30–42 points, and 2: <30 points.

Cystatin C: 0: ≤0.77 mg/L, 1: 0.78-0.92 mg/L, 2: >0.92mg/L

Fasting glucose: 0: <100 mg/dL, 1: 100-126 mg/dL, 2: ≥126 mg/dL (clinical cut-points suggested by the American Diabetes Association)

For the SBP and glucose components participants with treated or self-reported diagnosed hypertension or diabetes were coded into the least healthy tertile (5). At year 10 this included cumulative reports. The five components were summed to give a score of 0-10 for each participant at each time-point.

Mortality analysis

Participants were followed up for mortality from study inception until September 30th 2014. A summary of the study design and participant flow is given in Supplemental Figure S1. Survival analyses for the year 1 HAI were conducted from the date of the year 3 visit (when cystatin C was measured). 2264 participants with a year 3 cystatin C measurement, complete data on the other 4 HAI components at year 1 and mortality follow-up were included in this analysis. 1359 participants returned for a health assessment at year 10, of these 1122 with complete data for the HAI at year 1 and year 10 and mortality follow-up were included in these analyses. For the year

10 score and the change between years mortality follow-up was conducted from the date of the year 10 visit. . Follow-up days were defined as days from the relevant clinic visit until date of death or date of last contact, including all 17 years of the study. Deaths were ascertained from semi-annual contacts, reports from family members or review of obituaries and death records and adjudicated by committee from medical records, death certificate and informant interviews. Mean follow-up time from year 3 was 10.6 years with a maximum of 15.2 years. From year 10 the mean follow-up time was 6.2 years and the maximum 8.2 years.

Covariates

Demographic covariates included age (at year 1 or year 10), sex, self-reported race, study site and education. Further health related covariates were chosen based on prior work and known relationship to mortality from the selection of variables available at years 1 and 10 (2). These included smoking status, body mass index (BMI) and self-reported physical activity defined as kcal/kg/week from walking, stair climbing and chores (16, 17). 20m gait speed was included as a measure of functional ability and key health indicator. Prevalence of chronic health conditions was estimated at years 1 and 10 based on defined algorithms. A full description of the variables and their coding is included in Supplementary Material.

Statistical Analysis

Characteristics of the year 1 and year 10 samples were summarized as mean (SD) or median (IQR) for continuous variables and frequency (%) for categorical variables. Distributions of the HAI at year 1 and 10 were explored graphically and within person change calculated as year 10 score - year 1 score.

The relationships between the HAI at year 1 and year 10 and the change between years, and mortality were estimated from Cox proportional hazards models. The proportional hazards assumption was checked using the Schoenfield residuals test and comparison of fitted and observed survival curves. Model 1 included demographic variables: age, sex, race, study site and education. Model 2 additionally included BMI, smoking, physical activity, cancer, cardiovascular disease (CVD), pulmonary disease, depression, osteoporotic drug use and hip or knee osteoarthritis, and model 3 additionally included 20m gait speed. The full outputs from these models are included in supplemental tables S3-S5. Harrell's C statistics were calculated to compare different models at year 10.

Additional sets of models were constructed entering the change jointly with 1) the year 1 score and 2) the year 10 score. This allowed us to 1) account for the relationship between the change and the initial score and 2) assess the relative importance of the change and the current score.

The relationships between changes in the individual HAI components and mortality were modelled adjusting for the full set of covariates and for the year 10 score for that component.

All analyses were conducted using Stata version 14.1.

Results

The mean (SD) age of the sample at year 1 was 73.6 (2.8) years, 51.4% were female, 38.4% were black and 44.9% were educated above secondary level (Table 1). At year 10 the mean age of these participants was 82.1 (2.7), 50.5% had post-secondary education and 32.7% were black (Table 1). At year 1 they represented a healthier subset of the full sample with better scores on the HAI components (except SBP and fasting glucose) and lower levels of chronic disease (Table 1). As expected with increasing age the prevalence of chronic disease was generally higher and scores on the HAI components generally poorer at year 10.

The HAI was relatively normally distributed at both year 1 and year 10 (Figure 1A). In the matched year 1 and 10 sample, there was a shift from mainly lower scores at year 1 to higher scores at year 10 (Figure 1A). Within person change in the HAI was approximately normally distributed around a mean of 1.5, with about 3 quarters of the sample increasing their score over time (Figure 1B). Participants with lower scores tended to have greater increases while those with high scores remained more stable (Figure 1C).

Less than 10% of participants decreased their scores over time on any one component (Table S1). Consistent with previous reports of limited cross-sectional correlations between the HAI components (2, 3), correlations between component changes were low (-0.0461-0.1071, Table S2).

A total of 1436 deaths occurred during up to 15.2 years follow-up from year 3. 497 occurred after the year 10 assessment in the remaining sample. The mortality gradient across the range of the HAI was similar at year 1 and year 10 (Figure 2), increasing from 33 events per 1000 person years in participants with HAI scores ≤ 2 to 90 events per 1000 person years in participants with

scores of 7-10 at year 1 and from 33 to 100 across this range at year 10 (Table 2). This graded relationship remained after adjustment for demographic factors at both years (Hazard Ratio (95% Confidence Interval) for the highest (7-10) vs lowest (0-2) scores = 2.58 (2.10-3.18) at year 1 and 2.75 (1.68-4.48) at year 10). Hazard Ratios (95%CI) per unit higher HAI were 1.18 (1.14-1.21) at year 1 and 1.23 (1.17-1.29) at year 10. The relationships between the HAI and mortality tended to be slightly stronger after adjustment for chronic conditions and health behaviors (Table 2). This was due to the inclusion of BMI, which was positively related to several HAI components and negatively related to mortality. Further adjustment for gait speed slightly reduced the strength of relationships (Table 2).

The change in the HAI between years was also related to mortality (HR (95% CI)=1.08 (1.02-1.15) per unit increase in change score in the full models). Participants with the greatest increase had the highest mortality: HR(95%CI)=1.55 (1.11-2.16) in those gaining ≥4 points in the full models. Adjustment for the year 1 score increased the effect size for the change (HR(95%CI)=1.19 (1.11-1.27) per unit increase in the full models).

Inclusion of the year 10 score and the change in the same model attenuated the relationship with the change with little effect on the year 10 score relationship (HR(95%CI)=0.98 (0.92-1.05) for the change and HR(95%CI)=1.21 (1.14-1.29) for the year 10 score in the full models). C-statistics for the unadjusted year 10 score and change score models were 0.62 and 0.53 (Table S6). For the combined year 10 score and change model it was 0.62. The c-statistic for the model containing the year 10 score and all covariates was 0.7 and for a model containing all covariates without the HAI was 0.69.

One issue in constructing a HAI is whether to count known diagnoses of hypertension and diabetes as the highest score. Using the values for glucose and SBP without additionally scoring

the condition gave lower average scores at year 1 and 10 and a slightly reduced mean change score of 1.1 points. Mortality estimates were similar when these conditions were adjusted for in the full models, instead of included in the HAI (HR (95%CI) per unit = 1.13 (1.09-1.17) for year 1; 1.18 (1.11-1.25) for year 10; and 1.07 (1.01-1.14) for the change).

All HAI components were related to mortality from year 1 and year 10 in all models, except SBP at year 10 (Supplemental Table S7). However, of the change scores at year 10, only changes in DSST and cystatin C were related to mortality (HR (95%CI)=1.53 (1.33-1.75) and 1.14 (1.01-1.29) per unit increase in change score in demographic adjusted models, Table 3). These relationships were not greatly affected by adjustment for health covariates (Table 3). As for the overall change score, adjustment for year 1 score strengthened relationships with DSST (1.79 (1.54-2.09)), Cystatin C (1.30 (1.13-1.50)) and FVC (1.26 (1.08-1.47)) in demographic models (not shown). Adjustment for the year 10 scores attenuated the relationship with cystatin C and reduced the relationship with DSST (1.22 (1.03-1.46)). Changes in SBP and glucose did not clearly relate to mortality in any models (Table 3).

Discussion

Scores on a HAI increased at least 1 point over 9 years in 72% of adults aged in their 70s at baseline. The HAI score was related to mortality from year 1 and year 10. The change in HAI was also related to mortality, especially when accounting for differences in baseline score. Although this relationship could be attenuated by adjustment for year 10 score.

Some limitations of this study should be acknowledged. There was missing data for the HAI components at both years 1 and 10, substantial attrition due to mortality and other causes occurred before year 10 and not all remaining participants could complete a health assessment. This limits the generalizability of findings to less healthy older adults. Survival and other biases introduced from missing data might be expected to lead to underestimation of the relationship between HAI and mortality from year 10 and to limit variation in change scores. It was only possible to construct a full HAI at 2 time-points and cystatin C from year 3 had to be used for the year 1 score, limiting the scope of analyses possible. These limitations are balanced by important strengths of prospective measurement of the HAI, long term follow-up for repeat measurements and mortality and well-validated assessments of outcomes and confounding variables.

The HAI has been shown to stratify mortality rates in several samples of people aged 60 and older (4, 6, 8). Here we confirm it performs similarly in the older sample (mean age 82 years) remaining at year 10 of Health ABC. This effect was independent of known comorbidity and functional ability. Adding the HAI did not greatly increase the c-statistic for the full model. However, there is a limit to the classification accuracy achievable in epidemiological studies of complex outcomes and even apparently strong predictors may not increase these statistics for detailed models (18).

The raw change in HAI score was more modestly related to subsequent mortality. Survival bias is a partial explanation, with participants experiencing rapid increases in score not surviving to the second assessment. Additionally, interpreting change in longitudinal studies is complex. The change partly reflects the initial score, and the relevance of the change score is contextual with a small increase in a high score likely to capture a more serious or 'later' decline in health than a similar increase from a lower score. The availability of only 2 time points is particularly problematic as it is not possible to separate 'true' change processes from variations due to measurement error (and therefore regression to the mean), without at least a 3rd time point to estimate a trend. Adjustment for the initial score provides some accounting for these factors. After adjustment, the strength of relationship between the change and mortality reached a level comparable to the scores at year 1 or 10.

Our results overall show the HAI scores tend to increase with chronological age and variation in the change is related to subsequent mortality. These findings suggest the HAI is sensitive to physiologically relevant changes in health in aging, further supporting its utility as a measure of physiologic aging. However, adjustment for the year 10 score attenuated the relationship between the change and mortality. This implies, at least with the respect to mortality prediction, an individual's trajectory to their current score adds little prognostic information to the score itself. Clinically, this suggests a current measurement in itself would give a useful indication of possible health risks in cases where a longer history is unavailable.

Of the HAI components, only changes in DSST and cystatin C were related to mortality and only the DSST relationship remained after adjustment for year 10 score. Baseline measures of these variables have been identified as strong predictors of mortality in Health ABC (19). This heterogeneity of the change in HAI at the component level further helps to explain the more

modest relationship with mortality for the total change score. Blood pressure and glucose are extensively treated in this age group, making it more difficult to assess changes. The implications of these measures may also be different at advanced ages (20).

Future studies may usefully explore strategies to refine the HAI to optimally capture change, for example by focusing on the most informative components or through component weighting by mortality rates or functional ability (5, 21). Another important area is to analyze changes across larger numbers of time points. As well as mean changes this will allow derivation of indices of variability and classification of groups following different health trajectories to more completely capture the heterogeneity of health changes in aging (22-25).

In summary, HAI scores tended to increase with advancing age and predicted mortality from a given time-point, supporting the utility of the HAI as a summary measure of health in aging. Future studies to further characterize changes in the HAI and their relationships to health outcomes are warranted.

Funding

Health ABC was supported by NIA Contracts (N01-AG-6-2101, N01-AG-6-2103, N01-AG-6-2106, NIA grant R01-AG-028050, and NINR grant R01-NR-012459). MO'C is supported by an Ageing Research Leadership Fellowship awarded from the Centre for Ageing Research and Development in Ireland, which became the Ageing Research and Development Division within the Institute of Public Health in Ireland (IPH) in September 2015, sponsored by the American Federation for Aging Research Paul B Beeson Career Development Awards in Aging Research for the Island of Ireland. Dr. Kritchevsky is supported in part by the Wake Forest Older Americans Independence Center (P30 AG 21332) and Dr. Newman by the University of Pittsburgh Older Americans Independence Center (P30 AG024827).

References

1. Quan H, Li B, Couris CM, Fushimi K, Graham P, Hider P*, et al.* Updating and Validating the Charlson Comorbidity Index and Score for Risk Adjustment in Hospital Discharge Abstracts Using Data From 6 Countries. American Journal of Epidemiology. 2011;**173**:676-682. doi: 10.1093/aje/kwq433.
2. Sanders JL, Boudreau RM, Penninx BW, Simonsick EM, Kritchevsky SB, Satterfield S*, et al.* Association of a Modified Physiologic Index With Mortality and Incident Disability: The Health, Aging, and Body Composition Study. The Journals of Gerontology: Series A. 2012;**67**:1439-1446. doi: 10.1093/gerona/gls123.
3. Newman AB, Boudreau RM, Naydeck BL, Fried LF, Harris TB. A Physiologic Index of Comorbidity: Relationship to Mortality and Disability. The Journals of Gerontology: Series A. 2008;**63**:603-609. doi: 10.1093/gerona/63.6.603.
4. McCabe EL, Larson MG, Lunetta KL, Newman AB, Cheng S, Murabito JM. Association of an Index of Healthy Aging With Incident Cardiovascular Disease and Mortality in a Community-Based Sample of Older Adults. The Journals of Gerontology: Series A. 2016;**71**:1695-1701. doi: 10.1093/gerona/glw077.
5. Sanders JL, Minster RL, Barmada MM, Matteini AM, Boudreau RM, Christensen K*, et al.* Heritability of and Mortality Prediction With a Longevity Phenotype: The Healthy Aging Index. The Journals of Gerontology: Series A. 2014;**69**:479-485. doi: 10.1093/gerona/glt117.
6. Wu C, Smit E, Sanders JL, Newman AB, Odden MC. A Modified Healthy Aging Index and Its Association with Mortality: The National Health and Nutrition Examination Survey, 1999–2002. The Journals of Gerontology: Series A. 2017;**72**:1437-1444. doi: 10.1093/gerona/glw334.
7. Rosso AL, Sanders JL, Arnold AM, Boudreau RM, Hirsch CH, Carlson MC*, et al.* Multisystem Physiologic Impairments and Changes in Gait Speed of Older Adults. The Journals of Gerontology: Series A. 2015;**70**:319-324. doi: 10.1093/gerona/glu176.
8. Minster RL, Sanders JL, Singh J, Kammerer CM, Barmada MM, Matteini AM*, et al.* Genome-Wide Association Study and Linkage Analysis of the Healthy Aging Index. The Journals of Gerontology: Series A. 2015;**70**:1003-1008. doi: 10.1093/gerona/glv006.
9. Yeri A, Murphy RA, Marron MM, Clish C, Harris TB, Lewis GD*, et al.* Metabolite profiles of healthy aging index are associated with cardiovascular disease in African Americans: the Health, Aging, and Body Composition Study. The Journals of Gerontology: Series A. 2017:glx232-glx232. doi: 10.1093/gerona/glx232.
10. Espeland MA, Crimmins EM, Grossardt BR, Crandall JP, Gelfond JAL, Harris TB*, et al.* Clinical Trials Targeting Aging and Age-Related Multimorbidity. The Journals of Gerontology: Series A. 2017;**72**:355-361. doi: 10.1093/gerona/glw220.
11. Tampubolon G. Trajectories of the healthy ageing phenotype among middle-aged and older Britons, 2004–2013. Maturitas. 2016;**88**:9-15. doi: 10.1016/j.maturitas.2016.03.002.
12. Wilkie R, Tajar A, McBeth J. The Onset of Widespread Musculoskeletal Pain Is Associated with a Decrease in Healthy Ageing in Older People: A Population-Based Prospective Study. PLOS ONE. 2013;**8**:e59858. doi: 10.1371/journal.pone.0059858.
13. Goldenstein L, Driver TH, F. Fried L, Rifkin DE, Patel KV, Yenchek RH*, et al.* Serum Bicarbonate Concentrations and Kidney Disease Progression in Community-Living Elders: The Health, Aging, and Body Composition (Health ABC) Study. American Journal of Kidney Diseases. 2014;**64**:542-549. doi: 10.1053/j.ajkd.2014.05.009.
14. Bridevaux P-O, Dupuis-Lozeron E, Schindler C, Keidel D, Gerbase MW, Probst-Hensch NM*, et al.* Spirometer Replacement and Serial Lung Function Measurements in Population Studies: Results From the SAPALDIA Study. American Journal of Epidemiology. 2015;**181**:752-761. doi: 10.1093/aje/kwu352.

15. Tang W, Bentley AR, Kritchevsky SB, Harris TB, Newman AB, Bauer DC*, et al.* Genetic Variation in Antioxidant Enzymes, Cigarette Smoking and Longitudinal Change in Lung Function. Free radical biology & medicine. 2013;**63**:304-312. doi: 10.1016/j.freeradbiomed.2013.05.016.
16. Ainsworth BE, Haskell WL, Leon AS, Jacobs DR, Montoye HJ, Sallis JF*, et al.* Compendium of Physical Activities: classification of energy costs of human physical activities. Medicine & Science in Sports & Exercise. 1993;**25**:71-80. doi: 10.1249/00005768-199301000-00011.
17. Colbert LH, Visser M, Simonsick EM, Tracy RP, Newman AB, Kritchevsky SB*, et al.* Physical Activity, Exercise, and Inflammatory Markers in Older Adults: Findings from The Health, Aging and Body Composition Study. Journal of the American Geriatrics Society. 2004;**52**:1098-1104. doi: 10.1111/j.1532-5415.2004.52307.x.
18. Cook NR. Use and Misuse of the Receiver Operating Characteristic Curve in Risk Prediction. Circulation. 2007;**115**:928-935. doi: 10.1161/circulationaha.106.672402.
19. Swindell WR, Cummings SR, Sanders JL, Caserotti P, Rosano C, Satterfield S*, et al.* Data Mining Identifies Digit Symbol Substitution Test Score and Serum Cystatin C as Dominant Predictors of Mortality in Older Men and Women. Rejuvenation Research. 2012;**15**:405-413. doi: 10.1089/rej.2011.1297.
20. Ravindrarajah R, Hazra NC, Hamada S, Charlton J, Jackson SHD, Dregan A*, et al.* Systolic Blood Pressure Trajectory, Frailty and All-Cause Mortality Over 80 Years of Age. Cohort Study Using Electronic Health Records. Circulation. 2017. doi: 10.1161/circulationaha.116.026687.
21. Wei MY, Kabeto MU, Langa KM, Mukamal KJ. Multimorbidity and Physical and Cognitive Function: Performance of a New Multimorbidity-Weighted Index. The Journals of Gerontology: Series A. 2018;**73**:225-232. doi: 10.1093/gerona/glx114.
22. Arnold AM, Newman AB, Cushman M, Ding J, Kritchevsky S. Body Weight Dynamics and Their Association With Physical Function and Mortality in Older Adults: The Cardiovascular Health Study. The Journals of Gerontology: Series A. 2010;**65A**:63-70. doi: 10.1093/gerona/glp050.
23. Newman AB, Sanders JL, Kizer JR, Boudreau RM, Odden MC, Zeki Al Hazzouri A*, et al.* Trajectories of function and biomarkers with age: the CHS All Stars Study. International Journal of Epidemiology. 2016;**45**:10. doi: 10.1093/ije/dyw092.
24. Olaya B, Bobak M, Haro JM, Demakakos P. Trajectories of Verbal Episodic Memory in Middle-Aged and Older Adults: Evidence from the English Longitudinal Study of Ageing. Journal of the American Geriatrics Society. 2017;**65**:1274-1281. doi: 10.1111/jgs.14789.
25. Wu C, Shlipak MG, Stawski RS, Peralta CA, Psaty BM, Harris TB*, et al.* Visit-to-Visit Blood Pressure Variability and Mortality and Cardiovascular Outcomes Among Older Adults: The Health, Aging, and Body Composition Study. American Journal of Hypertension. 2017;**30**:151-158. doi: 10.1093/ajh/hpw106.

Tables

Table 1: Description of participants at year 1 and year 10

	Full sample	Year 10 sample	
	year 1	year 1	year 10
n	2264	1122	1122
HA Index & components			
HA Index score	4.8 (2.2)	4.3 (2.1)	5.7 (2.1)
Systolic blood pressure, mmHG, mean (SD)	135.4 (20.5)	135.3 (20.1)	135.0 (19.0)
Forced vital capacity, mL, mean (SD)	2890.9 (824.2)	2974.3 (800.1)	2606.8 (789.3)
Digit symbol substitution test, points, mean (SD)	36.5 (14.4)	39.9 (13.6)	34.5 (14.1)
Serum cystatin C*, mg/dL, mean (SD)	0.89 (0.28)	0.84 (0.18)	0.96 (0.33)
Serum fasting glucose, mg/dL, mean (SD)	103.8 (33.7)	101.1 (29.9)	100.8 (24.5)
Covariates			
Age, years, mean (SD)	73.6 (2.8)	73.1 (2.7)	82.1 (2.7)
Female, n (%)	1164 (51.4)	594 (52.9)	-
Black race, n (%)	870 (38.4)	367 (32.7)	-
Pittsburgh site, n (%)	1172 (51.8)	599 (53.4)	-
Post secondary education, n (%)	1013 (44.9)	567 (50.5)	-

Body Mass Index, kg/m^2, mean (SD)	27.3 (4.7)	27.3 (4.6)	27.1 (4.8)
Physical activity**, kcal/kg/week, median (IQR)	10.5 (3.5-24.3)	12.2 (4.2-26.2)	3.8 (0.5-11.6)
20m gait speed, m/s, mean(SD)***	1.3 (0.3)	1.4 (0.3)	1.0 (0.2)
Current smoker, n (%)	210 (9.3)	69 (6.2)	37 (3.3)
Cancer, n (%)	381 (16.9)	167 (14.9)	276 (24.6)
Cardiovascular disease, n (%)	592 (26.7)	250 (22.7)	368 (32.8)
Pulmonary disease, n (%)	242 (10.8)	90 (8.1)	144 (13.0)
Depression (CES-D ≥10), n (%)	114 (5.1)	33 (3.0)	145 (13.4)
Osteoporotic drug, n (%)	101 (4.5)	49 (4.4)	166 (14.8)
Hip or knee osteoarthritis, n (%)	253 (11.3)	134 (12.1)	346 (31.0)
Hypertension****, n (%)	1124 (50.0)	520 (46.6)	776 (69.2)
Diabetes****, n (%)	325 (14.4)	125 (11.2)	185 (16.5)

*From year 3

**kcal/kg/week from walking, stairs & chores

***From 2 minute walk at year 1 (n=2029)

****From self-reported diagnosis or medication use

Table 2: Hazard ratios for Mortality by Healthy Aging Index scores from year 1, year 10 and the change between years

	Events/1000 person years	Model 1	Model 2	Model 3
HA index score yr 1				
Mortality from yr 3-17 (N=1436z/2264d)				
HR per unit index		1.18 [1.14,1.21]	1.19 [1.15,1.23]	1.17 [1.13,1.21]
HA index score				
0-2 (n=138z/333d)	33	1	1	1
3-4 (n=384z/677d)	49	1.39 [1.14,1.69]	1.42 [1.16,1.74]	1.39 [1.13,1.71]
5-6 (n=502z/737d)	67	1.91 [1.57,2.33]	1.94 [1.59,2.38]	1.81 [1.46,2.24]
7-10 (n=412z/517d)	90	2.58 [2.10,3.18]	2.70 [2.17,3.36]	2.45 [1.94,3.08]
HA index score yr 10				
Mortality from yr 10-17 (N=497z/1122d)				
HR per unit index		1.23 [1.17,1.29]	1.24 [1.18,1.31]	1.20 [1.14,1.27]
HA index score				
0-2 (n=18z/78d)	33	1	1	1
3-4 (n=70z/237d)	43	1.24 [0.74,2.09]	1.39 [0.80,2.41]	1.39 [0.80,2.40]
5-6 (n=163z/368d)	70	1.95 [1.19,3.20]	2.26 [1.34,3.84]	2.05 [1.21,3.47]
7-10 (n=246z/439d)	100	2.75 [1.68,4.48]	3.18 [1.87,5.39]	2.66 [1.57,4.52]
HA index change yr1-10				
Mortality from yr 10-17 (N=497z/1122d)				
HR per unit change		1.09 [1.03,1.16]	1.08 [1.02,1.14]	1.08 [1.02,1.15]

HA index change score				
-4-0 (n=124z/311d)	63	1	1	1
1 (n=125z/291d)	69	1.13 [0.88,1.45]	1.18 [0.91,1.53]	1.24 [0.95,1.61]
2-3 (n=186/411d)	73	1.15 [0.91,1.44]	1.13 [0.89,1.44]	1.24 [0.97,1.59]
4-8 (n=62z/109d)	102	1.77 [1.30,2.41]	1.62 [1.17,2.25]	1.55 [1.11,2.16]
HA index change yr 1-10 and score at yr 1				
HR per unit change		1.21 [1.14,1.29]	1.21 [1.13,1.30]	1.19 [1.11,1.27]
HR per unit yr 1 score		1.24 [1.17,1.30]	1.27 [1.19,1.35]	1.21 [1.14,1.29]
HA index change yr 1-10 and score at yr 10				
HR per unit change		0.98 [0.92,1.04]	0.95 [0.89,1.02]	0.98 [0.92,1.05]
HR per unit yr 10 score		1.24 [1.17,1.30]	1.27 [1.19,1.35]	1.21 [1.14,1.29]

Model 1: age, sex, site, race, education

Model 2: Model 1 + BMI, smoking, physical activity, cancer, cardiovascular disease, pulmonary disease, depression, osteoporotic drugs and hip or knee osteoarthritis,

Model 3: Model 2 + gait speed

Table 3: Changes in Healthy Aging Index components and mortality

HAI component	Events/1000 person years	Model 1	Model 2	Model 3
Mortality from yr 10-17 (N=497/1122)				
SBP				
HR per unit change		0.90 [0.79,1.02]	0.90 [0.79,1.03]	0.87 [0.75,1.00]
Change score				
-1/-2 (n=28z/61d)	77	1	1	1
0 (n=351z/772d)	74	1.02 [0.69,1.50]	0.97 [0.64,1.46]	0.77 [0.48,1.24]
1 (n=81z/191d)	67	0.86 [0.55,1.32]	0.96 [0.61,1.52]	0.78 [0.47,1.29]
2 (n=37z/98d)	58	0.81 [0.50,1.34]	0.70 [0.42,1.18]	0.54 [0.30,0.96]
FVC				
HR per unit change		1.08 [0.94,1.24]	1.08 [0.94,1.25]	0.96 [0.82,1.13]
Change score				
-1/-2 (n=21z/45d)	75	1	1	1
0 (n=265z/591d)	73	1.07 [0.69,1.69]	0.97 [0.61,1.55]	0.82 [0.51,1.32]
1 (n=175z/421d)	66	1.05 [0.66,1.66]	0.98 [0.61,1.58]	0.74 [0.45,1.23]
2 (n=36z/65d)	96	1.56 [0.90,2.70]	1.40 [0.79,2.51]	0.94 [0.51,1.76]
DSST				

HR per unit change		1.53 [1.33,1.75]	1.41 [1.21,1.63]	1.22 [1.03,1.46]
Change score				
-1/-2 (n=20z/82d)	35	1	1	1
0 (n=275z/669d)	64	1.74 [1.10,2.74]	1.87 [1.14,3.08]	1.71 [1.04,2.82]
1 (n=178z/336d)	92	2.44 [1.54,3.89]	2.45 [1.47,4.05]	1.88 [1.10,3.21]
2 (n=24z/35d)	150	4.64 [2.56,8.42]	3.63 [1.86,7.08]	2.51 [1.23,5.11]
Cystatin C				
HR per unit change		1.14 [1.01,1.29]	1.15 [1.01,1.31]	1.04 [0.90,1.21]
Change score				
-1/-2 (n=43z/99d)	72	1	1	1
0 (n=279z/665d)	67	0.96 [0.69,1.32]	0.96 [0.68,1.34]	0.85 [0.60,1.21]
1 (n=136z/287d)	76	1.08 [0.77,1.53]	1.10 [0.77,1.58]	0.89 [0.60,1.32]
2 (n=39z/71d)	103	1.50 [0.97,2.31]	1.48 [0.93,2.36]	1.10 [0.66,1.84]
Glucose				
HR per unit change		1.01 [0.88,1.17]	1.02 [0.87,1.19]	0.86 [0.72,1.03]
Change score				
-1/-2 (n=41z/89d)	74	1	1	1
0 (n=342z/793d)	70	0.96 [0.69,1.33]	1.08 [0.74,1.56]	0.98 [0.67,1.42]
1 (n=99z/206d)	78	1.00 [0.69,1.44]	1.12 [0.75,1.69]	0.84 [0.54,1.30]

2 (n=15z/34d)	69	1.00 [0.55,1.82]	0.96 [0.50,1.85]	0.60 [0.29,1.20]

Model 1: age, sex, site, race, education

Model 2: Model 1 + BMI, smoking, physical activity cancer, cardiovascular disease, pulmonary disease, depression, osteoporotic drugs, hip or knee osteoarthritis and gait speed

Model 3: Model 2 + year 10 score for that component

Figures

Figure 1: Summaries of changes in a Healthy Aging Index over 9 years

1A: Distribution of the HAI at year 1 and year 10

1B: Distribution of the change in HAI scores

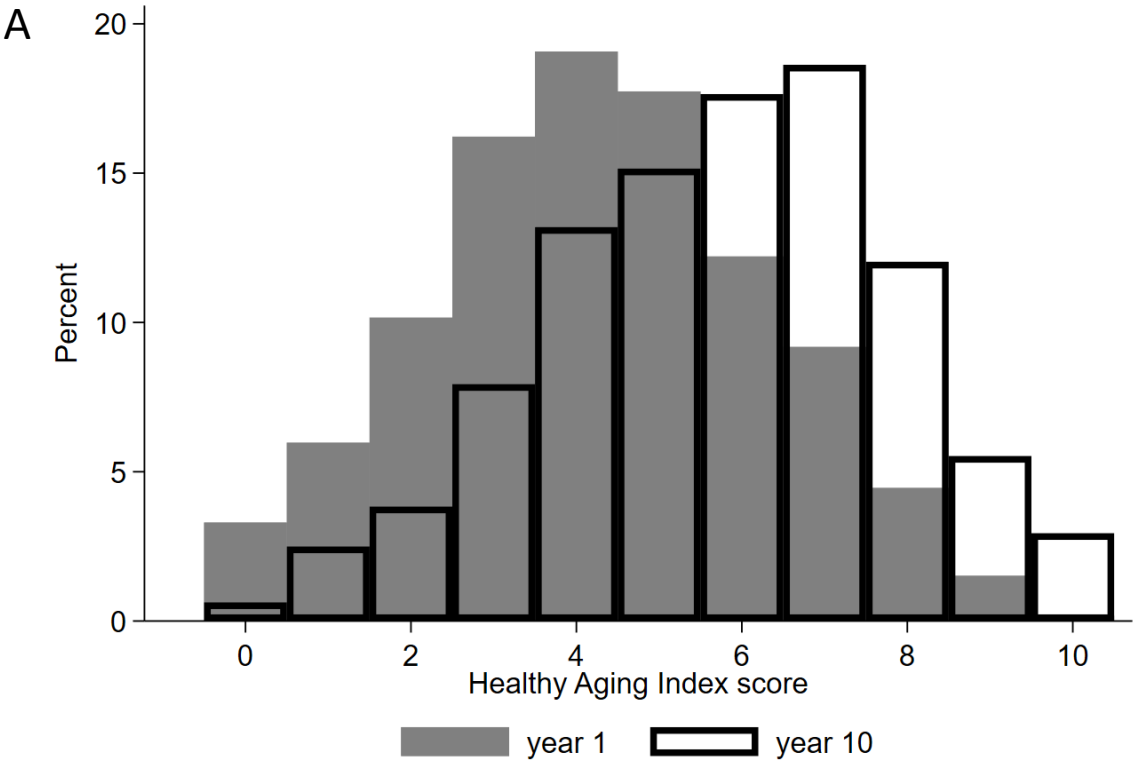
1C: Mean changes in HAI by baseline score

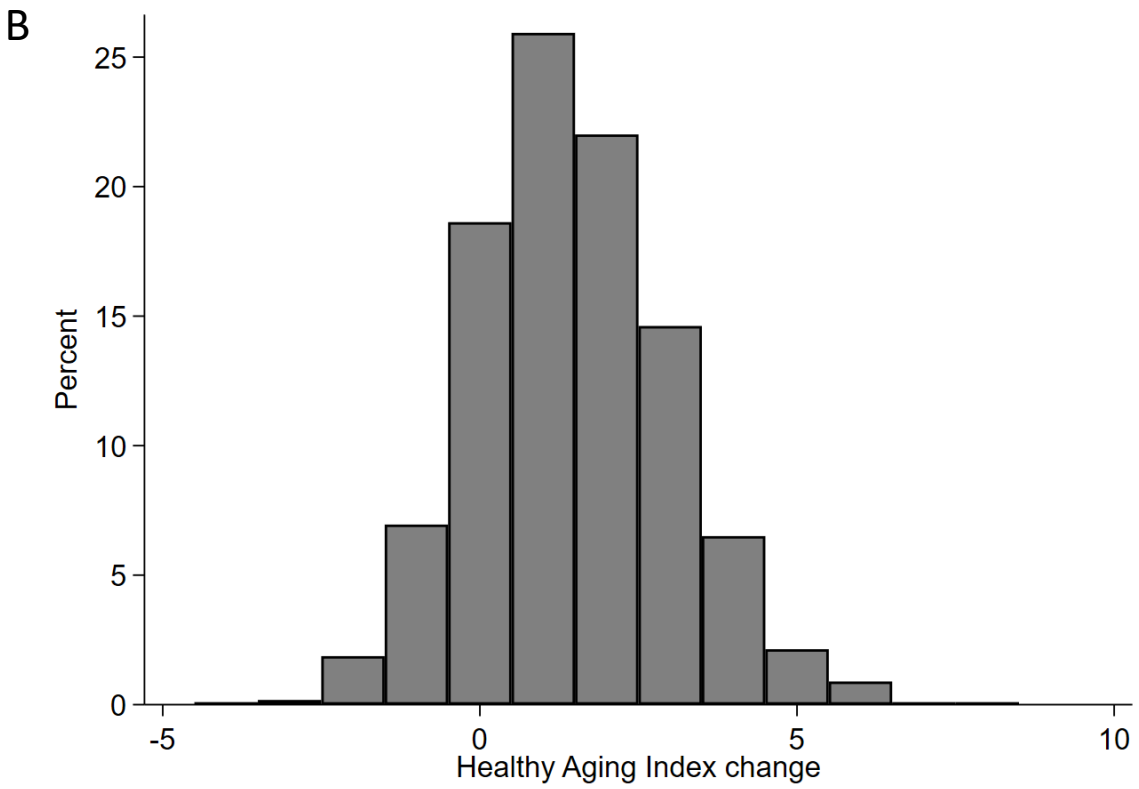
Figure 2: Kaplan-Meier survival curves for Healthy Aging Index scores for year 1, year 10 and the change between years

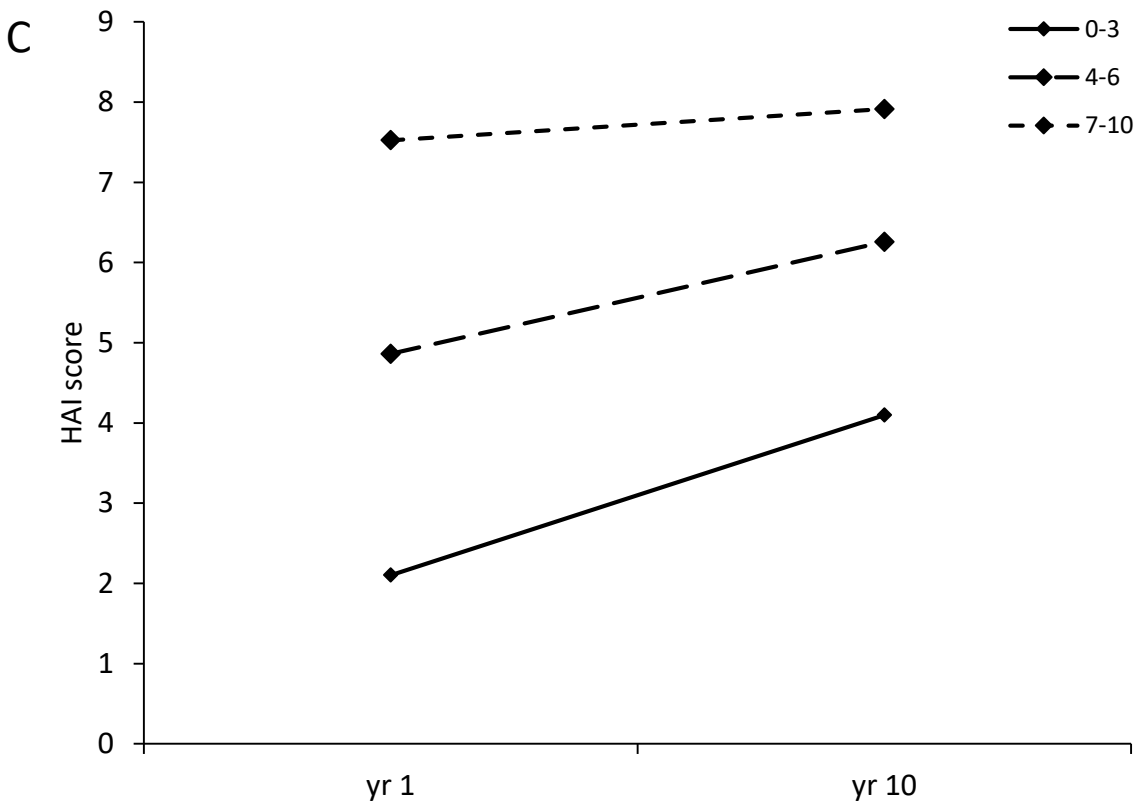
2A: Mortality by HAI score from year 1

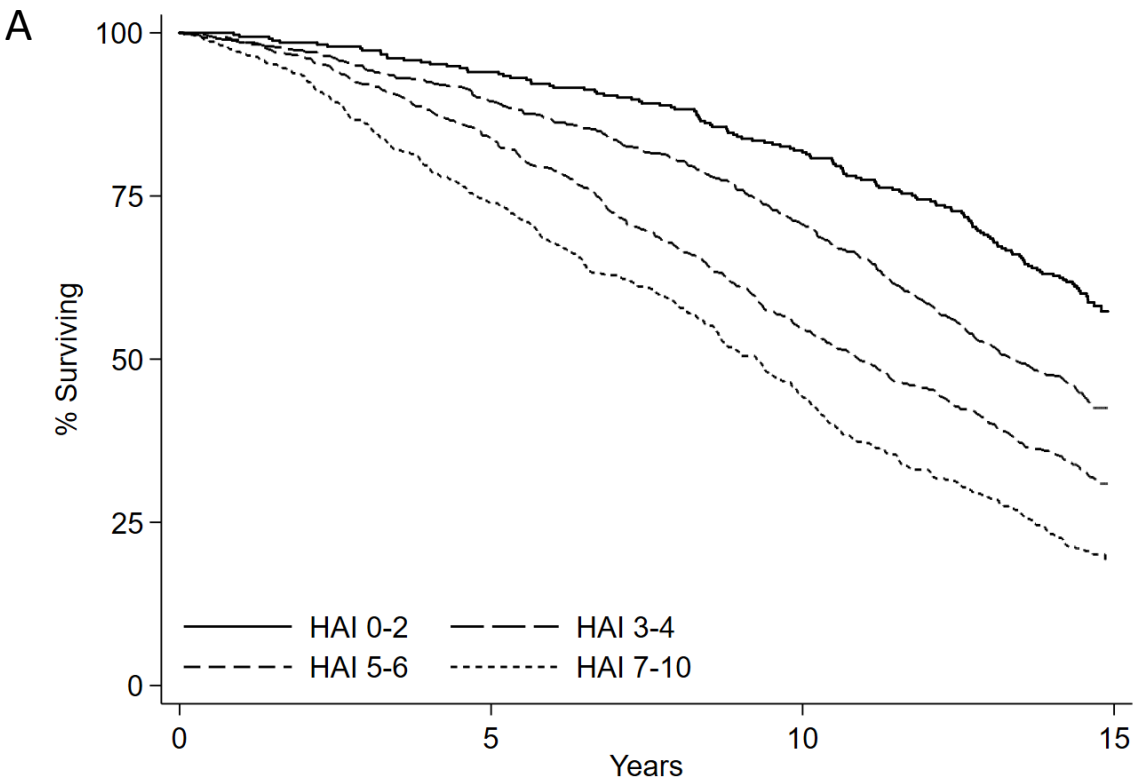
2B: Mortality by HAI score from year 10

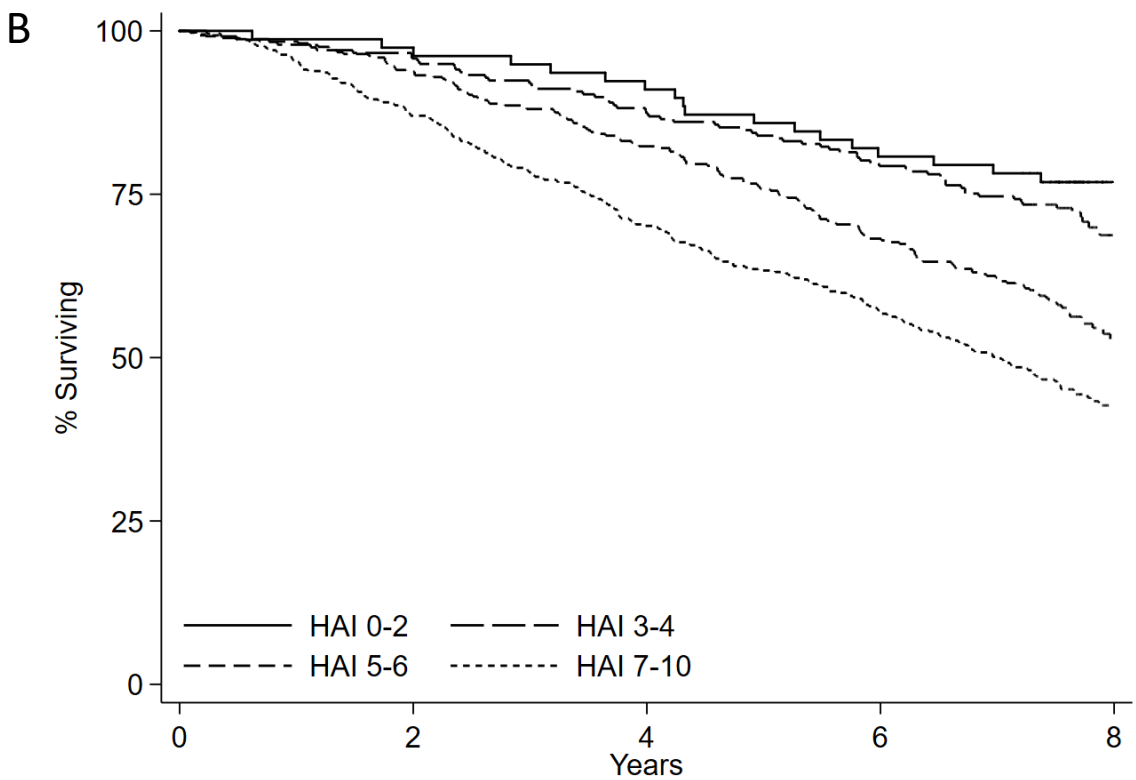
2C: Mortality by HAI change score between years

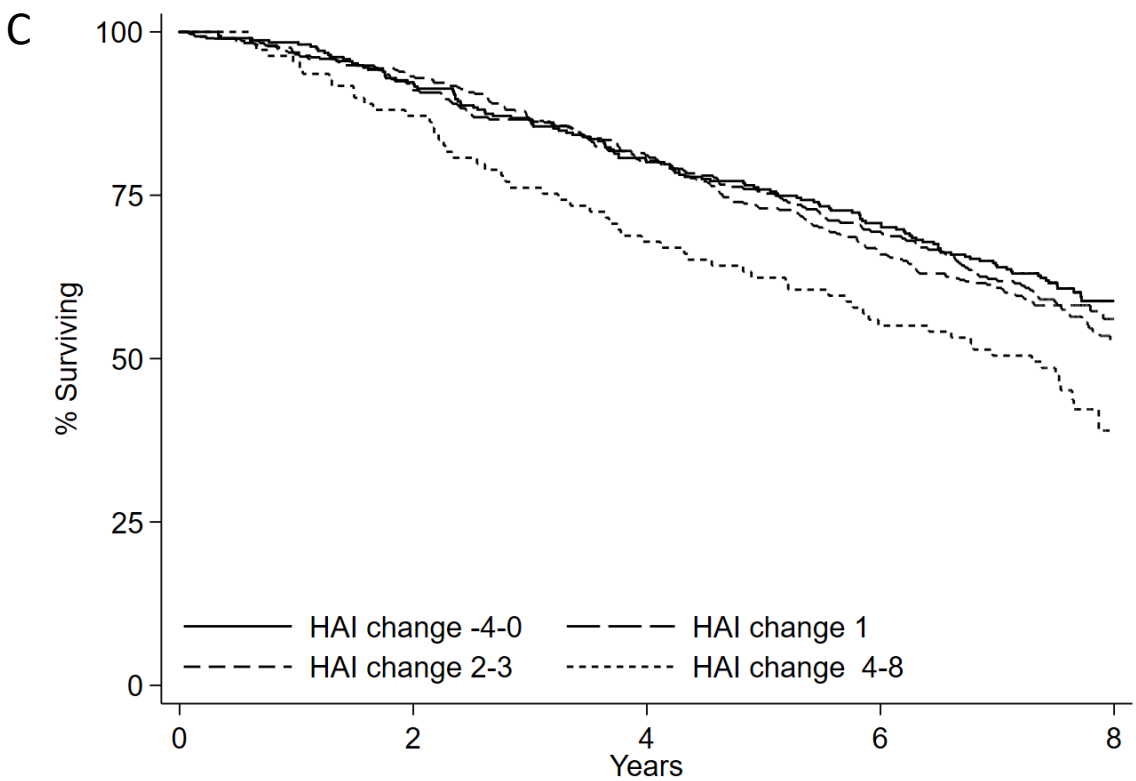

A
Percent
0
5
10
15
20
0
2
4
6
8
10
Healthy Aging Index score
year 1
year 10


B
Percent
0
5
10
15
20
25
-5
0
5
10
Healthy Aging Index change


C
HAI score
0
1
2
3
4
5
6
7
8
9
yr 1
yr 10
0-3
4-6
7-10


A
100
75
50
25
0
% Surviving
HAI 0-2
HAI 3-4
HAI 5-6
HAI 7-10
0
5
10
15
Years


B
100
75
50
25
0
% Surviving
HAI 0-2
HAI 3-4
HAI 5-6
HAI 7-10
0
2
4
6
8
Years


C
100
75
50
25
0
% Surviving
HAI change -4-0
HAI change 1
HAI change 2-3
HAI change 4-8
0
2
4
6
8
Years